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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/031,414	05/29/2002	Karin Briner	X-11593	2062

25885 7590 09/04/2003

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EXAMINER
MCKENZIE, THOMAS C

ART UNIT	PAPER NUMBER
1624	

DATE MAILED: 09/04/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	10/031,414	BRINER ET AL.	
	Examiner	Art Unit	
	Thomas McKenzie Ph.D.	1624	

-- The MAILING DATE of this communication appears on the cover sh et with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 May 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1,2,4,5,7,8 and 11-20* is/are allowed.

6)☒ Claim(s) *3,6,9 and 10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. This action is in response to an application filed on 5/29/02. There are twenty claims pending and twenty under consideration. Claims 1 and 11-20 are compound claims. Claim 2 is a composition claim. Claims 3-10 are use claims. This is the first action on the merits. The application concerns some piperidine substituted benzofuran compounds, compositions, and uses thereof.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3 and 6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is unclear who is in need of activation of their 5-HT_{2C} receptors. Since Applicants' compounds are agonists at this serotonin receptor subtype, crudely put, are stimulants. Is it possible that everyone might feel the need of such stimulation? There is a list of possible diseases associated with the receptor given in lines 21-31, page 3. However, the list uses open language. What other diseases are Applicants intending to treat? The specification does not set forth any steps involved in determining how to identify "a mammal in need of such activation". It is unclear what diseases and treatments applicant is intending to encompass. Determining whether a given disease

responds or does not respond to such a receptor agonist and thus, covered by the claim language, will require extensive and potentially inconclusive clinical research. With out such clinical research to identify the patients and diseases Applicants intend to treat, the physician skilled in the clinical arts cannot determine the metes and bounds of the claim. Hence, the claim is indefinite.

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 3, 6, 9, and 10 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating obesity and depression, does not reasonably provide enablement for treating obsessive compulsive disorders or for stimulating 5-HT_{2C} receptors in mammals generally. The specification does not enable any physician skilled in the art of medicine, to make the invention commensurate in scope with these claims. The how to make portion of the statute, when applied to a use claim means making the claimed process work. "The factors to be considered [in making an enablement rejection] have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the

predictability or unpredictability of the art and the breadth of the claims", *In re Rainer*, 146 USPQ 218 (1965); *In re Colianni*, 195 USPQ 150, *Ex parte Formal*, 230 USPQ 546.

a) Determining if any particular claimed compound would treat any particular 5-HT_{2C} receptor related disease would require synthesis of the compound, formulation into a suitable dosage form, and subjecting it clinical trials with a number of fundamentally different diseases described above in the indefiniteness rejection, or to testing them in an assay known to be correlated to clinical efficacy of such treatment. This is a large degree of experimentation. b) The direction concerning treating 5-HT_{2C} receptor related diseases is found in lines 21-31, page 3, which merely states Applicants' intention to do so. Applicants describe formulations in the passage spanning line 26, page 130 to line 23, page 132. Applicants have provided ten working examples of formulated compounds. Doses required to practice their invention are described in lines 24-29, page 130. A 3,000-fold range of doses is recommended. Since no 5-HT_{2C} receptor agonist has ever been used to treat obsessive compulsive disorders, how is the skilled physician to know what dose to use? There are two *in vitro* assays described in the passage spanning line 26, page 127 to line 5, page 130 with no data but it is unclear if these assay is correlated to obsessive compulsive disorders or to the other

possible diseases to be treated. There is an *in vivo assay* drawn to obesity treatment described in lines 10-24, page 130, again with no data, but any connection of this assay to obsessive compulsive disorders is obscure. c) There is no working example of treatment of any disease in man or animals. d) The nature of the invention is clinical treatment of disease, which involves physiological activity. e) The state of the clinical arts in 5-HT_{2C} receptor related diseases is provided by Robichaud (Ann. Reports Med. Chem.) who reports in the third paragraph on page 14 that the only clinical study underway in 2000 for such agents was for depression and anxiety. Other clinical indications were only "potential". In the second paragraph on page 11, art-recognition for uses in depression and obsetity of serotoniergic agents is reported.

f) The artisan using Applicants invention would be a physician with a MD degree, board certified in psychiatry, and with several years of experience. g) It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved", and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). h) The scope of the claims involves all of the thousands of compounds of claim a as well as the unknown of diseases embraced by claim 3. Thus, the scope of claims is very broad.

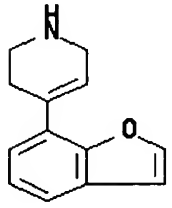
MPEP §2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here and undue experimentation will be required to practice Applicants' invention.

4. Claims 3 and 6 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention. The how to use portion of the statute means that Applicants must teach the skilled practitioner, in this case a physician, why to practice the claimed process. The physician clearly must know what disease and what symptoms she is to treat. The rejected claims are drawn to treatment of 5-HT_{2C} receptor related diseases, which as recited reads on the treatment of any and all diseases for which there is no enabling disclosure. This scope of disease treatment is not adequately supported based solely on the testing data provided in the specification at pages 127-130. The specification at pages 3 asserts that the compounds are useful for

treating all sorts of diseases for which Applicants have provided no empirical support. A recent review of Robichaud (Ann. Reports Med. Chem.) states that use of such 5-HT_{2C} receptor agonists is still in the experimental stage and is speculative in nature. Substantiation of use and scope is required when the use is "speculative", "sufficiently unusual", or not provided in the specification, *Ex parte Jovanovics,* 211 USPQ 907, *In re Langer,* 183 USPQ 288, *Hoffman v. Klaus*, 9 USPQ2d 1657, and *Ex parte Powers*, 200 USPQ 925 concerning the type of testing needed to support *in vivo* use claims. Also see the MPEP § 2164.03 for enablement requirements in the structure sensitive arts of pharmacology and medicinal chemistry.

Allowable Subject Matter

5. Claims 1, 2, 4, 5, 7, 8, and 11-20 are allowed. While Kohlman (EP 982,304 A1) teaches piperidine compounds lacking Applicants required substituent, exemplified by the compound below, these compounds in the reference are chemical intermediates. Apart from the lack of any teaching to add Applicants required wmthyl groups, these intermediates cannot form the basis of any obviousness rejection.



Conclusion

6. Please direct any inquiry concerning this communication or earlier communications from the Examiner to Thomas C McKenzie, Ph. D. whose telephone number is (703) 308-9806. The FAX number for amendments is (703) 872-9306. The PTO presently encourages all applicants to communicate by FAX. The Examiner is available from 8:30 to 5:30, Monday through Friday. If attempts to reach the Examiner by telephone are unsuccessful, you can reach the Examiner's supervisor, Mukund Shah at (703) 308-4716. Please direct general inquiries or any inquiry relating to the status of this application to the receptionist whose telephone number is (703) 308-1235.

Thomas C. McKenzie, Ph.D.
Patent Examiner
Art Unit 1624

TCMcK